Anticholinergic medications, benzodiazepines and long-term cognitive decline in large observational studies

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Findings from the Anticholinergics, Benzodiazepines, Cognition and Dementia (ABCD) study

Objectives
To determine whether the rate of dementia and cognitive decline is greater among older adults taking the following commonly used medicines:
- Anticholinergic medications - used for depression, overactive bladder, Parkinson’s disease, allergies, stomach cramps, and psychosis.
- Benzodiazepines - used for anxiety and sleep disturbance
- Z-drugs (zolpidem, zopiclone and zaleplon) - used for sleep disturbance

Medications and risk of dementia

Primary care data
We used UK primary care data to examine the 20 year medication history of 40,770 patients newly diagnosed with dementia compared to 283,933 age and sex matched patients without dementia.
Dementia patients were 11% more likely to have history of anticholinergic use. However associations were inconsistent across drug classes (figure 1).
No association with benzodiazepines/Z-drugs and dementia risk.

Medications and cognitive decline

Classifying anticholinergic medications
- The anticholinergic burden scale (ACB) measures the total amount of anticholinergic medication being used by an individual, and the evidence of their anticholinergic activity rated as 0, 1, 2, or 3.
- We classified medications with an ACB score of 3 as anticholinergic (“clinically relevant anticholinergic effects and reported associations with delirium”)
- ACB scale: www.agingbraincare.org/tools/abc-anticholinergic-cognitive-burden-scale/

MRC Cognitive Function and Ageing Study
13,004 participants aged 65+ years with 10-year follow-up
We observed 0.11 (p<0.01) greater decline in mini-mental state examination score (MMSE) per year when taking anticholinergics at baseline (figure 2).
We observed no greater decline in MMSE when taking benzodiazepines/Z-drugs at baseline.

Systematic reviews
Two systematic reviews identified 44 studies examining benzodiazepine and anticholinergic medication use and cognitive decline and dementia. The majority reported that greater benzodiazepine and anticholinergic medication use was associated with more cognitive decline and dementia, however studies varied in the size of the effect and in their quality. There are substantial inconsistencies in the overall evidence regarding the association between dementia and use of anticholinergics or benzodiazepines.

Conclusions
In the largest studies to date, our analyses suggest that benzodiazepines and anticholinergic medications affect cognition over the short-term. We observed no long-term dementia risk with benzodiazepine or Z-drug use, but small associations between certain anticholinergics (antidepressants, antiparkinsons, and urological drugs) and dementia that warrant further research.